Patent Claims

1. An isolated polynucleotide comprising

    i) a first nucleotide sequence encoding at least one regulator of morphology capable of regulating the morphology of a dimorphic fungal cell, and operably linked thereto

    ii) a second nucleotide sequence comprising an expression signal capable of directing the expression of the first nucleotide sequence in a dimorphic fungal cell,

    wherein the first and second nucleotide sequences are not natively associated.

2. Polynucleotide according to claim 1, wherein the dimorphic fungal cell is capable of growing as a multinucleated cell having a unicellular, essentially spherical morphology and/or capable of growing as a mycelium having a filamentous structure and comprising multinucleated cells.

3. Polynucleotide according to claim 2, wherein the multinucleated cells are multipolar.

4. Polynucleotide according to claim 2, wherein the dimorphic fungal cell belongs to the class of Zygomycetes.

5. Polynucleotide according to claim 4, wherein the dimorphic fungal cell belongs to the order of Mucorales.

6. Polynucleotide according to claim 4, wherein the dimorphic fungal cell belongs to a genus selected from the group of genera consisting of Mucor, Thermomucor, Rhizomucor, Mycotypha, Rhizopus, and Cokeromyces.

7. Polynucleotide according to claim 4, wherein the dimorphic fungal cell belongs to the genus Mucor.

8. Polynucleotide according to claim 4, wherein the dimorphic fungal cell is a Mucor species selected from the group of Mucor species consisting of M. circinelloides, M. hiemalis, M. rouxii, M. genevensis, M. bacilliformis, and M. subtillissimus.

9. Polynucleotide according to claim 8, wherein the Mucor species is M. circinelloides.

10. Polynucleotide according to claim 1, wherein the dimorphic fungal cell is capable of growing as a uninucleated cell having a unicellular, essentially spherical morphology, and/or capable of growing as a filamentous structure comprising uninucleated cells.

11. Polynucleotide according to claim 10, wherein the dimorphic fungal cell is selected from the group consisting of Yarrowia, Candida and Arxula.

12. Polynucleotide according to claim 1, wherein the first nucleotide sequence is selected from the group consisting of

i) a polynucleotide comprising nucleotides 542 to 1930 of SEQ ID NO:1, and

ii) a polynucleotide comprising or essentially consisting of the coding sequence of *pkaR* encoding the regulatory subunit of protein kinase A (PKAR) of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14062; and

iii) a polynucleotide encoding a polypeptide having the amino acid sequence as shown in SEQ ID NO:2; and

iv) a polynucleotide encoding a fragment of a polypeptide encoded by polynucleotides (i), (ii) or (iii), wherein said fragment

a) has Mucor circinelloides protein kinase A regulatory subunit acitivty and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a cAMP binding domain of Mucor circinelloides protein kinase A, wherein said cAMP binding domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:2; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:2 for binding to at least one predetermined binding partner, including cAMP and/or the catalytic subunit for protein kinase A; and

v) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) (iii), and (iv), and encodes a polypeptide that

a) has Mucor circinelloides protein kinase A regulatory subunit acitivty and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a cAMP binding domain of Mucor circinelloides protein kinase A, wherein said cAMP binding domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:2; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:2 for binding to at least one predetermined binding partner, including cAMP and/or the catalytic subunit for protein kinase A; and

vi) a polynucleotide comprising a nucleotide sequence which is degenerate to the nucleotide sequence of a polynucleotide as defined in any of (iv) and (v),

and the complementary strand of such a polynucleotide.

13. Polynucleotide according to claim 1, wherein the first nucleotide sequence comprises nucleotides 542 to 1930 of SEQ ID NO:1.

14. Polynucleotide according to claim 1, wherein the first nucleotide sequence comprises or essentially consists of the coding sequence of *pkaR* encoding the regulatory subunit of protein kinase A (PKAR) of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14062.

15. Polynucleotide according to claim 1, wherein the first nucleotide sequence encodes a polypeptide having the amino acid sequence as shown in SEQ ID NO:2.

16. Polynucleotide according to claim 1, wherein the first nucleotide sequence encodes a fragment of the polypeptide having the amino acid sequence as shown in SEQ ID NO:2, wherein said fragment

a) has Mucor circinelloides protein kinase A regulatory subunit acitivty and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a cAMP binding domain of Mucor circinelloides protein kinase A, wherein said cAMP binding domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:2; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:2 for binding to at least one predetermined binding partner, including cAMP and/or the catalytic subunit for protein kinase A.

17. Polynucleotide according to claim 1, wherein the complementary strand of said polynucleotide hybridizes under stringent conditions with the polynucleotide according to any of claims 13 to 16 and encodes a polypeptide that

a) has Mucor circinelloides protein kinase A regulatory subunit acitivty and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a cAMP binding domain of Mucor circinelloides protein kinase A, wherein said cAMP binding domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:2; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:2 for binding to at least one predetermined binding partner, including cAMP and/or the catalytic subunit for protein kinase A.

18. Polynucleotide according to claim 1 and comprising a nucleotide sequence which is degenerate to the first nucleotide sequence according to any of claims 16 and 17.

19. Polynucleotide according to claim 12, said polynucleotide comprising the complementary strand of the polynucleotide according to any of claims 12 to 18.

20. Polynucleotide according to claim 1, wherein the first nucleotide sequence is selected from the group consisting of

i) a polynucleotide comprising nucleotides 534 to 2471 of SEQ ID NO:11, and

ii) a polynucleotide comprising or essentially consisting of the coding sequence of *pkaC* encoding a catalytic subunit of protein kinase A (PKAC) of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14839; and

iii) a polynucleotide encoding a polypeptide having the amino acid sequence as shown in SEQ ID NO:12; and

iv) a polynucleotide encoding a fragment of a polypeptide encoded by polynucleotides (i), (ii) or (iii), wherein said fragment

a) has Mucor circinelloides catalytic subunit of protein kinase A activity and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a protein kinase A binding domain of Mucor circinelloides PKAC, wherein said domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:12; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:12 for binding to at least one predetermined binding partner, including PKAR; and

v) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) (iii), and (iv), and encodes a polypeptide that

a) has Mucor circinelloides catalytic subunit of protein kinase A activity and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a protein kinase A binding domain of Mucor circinelloides PKAC, wherein said domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:12; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:12 for binding to at least one predetermined binding partner, including PKAR; and

vi) a polynucleotide comprising a nucleotide sequence which is degenerate to the nucleotide sequence of a polynucleotide as defined in any of (iv) and (v),

and the complementary strand of such a polynucleotide.

21. Polynucleotide according to claim 1, wherein the first nucleotide sequence comprises nucleotides 534 to 2471 of SEQ ID NO:11.

22. Polynucleotide according to claim 1, wherein the first nucleotide sequence comprises or essentially consists of the coding sequence of *pkaC* encoding a catalytic subunit of protein kinase A (PKAC) of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14839.

23. Polynucleotide according to claim 1, wherein the first nucleotide sequence encodes a polypeptide having the amino acid sequence as shown in SEQ ID NO:12.

24. Polynucleotide according to claim 1, wherein the first nucleotide sequence encodes a fragment of the polypeptide having the amino acid sequence as shown in SEQ ID NO:12, wherein said fragment

a) has Mucor circinelloides catalytic subunit of protein kinase A activity and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a protein kinase A binding domain of Mucor circinelloides PKAC, wherein said domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:12; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:12 for binding to at least one predetermined binding partner, including PKAR.

25. Polynucleotide according to claim 1, wherein the complementary strand of said polynucleotide hybridizes under stringent conditions with the polynucleotide according to any of claims 21 to 24 and encodes a polypeptide that

a) has Mucor circinelloides catalytic subunit of protein kinase A activity and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a protein kinase A binding domain of Mucor circinelloides PKAC, wherein said domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:12; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:12 for binding to at least one predetermined binding partner, including PKAR.

26. Polynucleotide according to claim 1 and comprising a nucleotide sequence which is degenerate to the first nucleotide sequence according to any of claims 24 and 25.

27. Polynucleotide according to claim 20, said polynucleotide comprising the complementary strand of the polynucleotide according to any of claims 21 to 26.

28. Polynucleotide according to claim 1, wherein said first and/or second nucleotide sequence is derived from a microbial cell.

29. Polynucleotide according to claim 28, wherein said microbial cell is selected from the group of microbial cells consisting of eukaryotic microbial cells and procaryotic cells.

30. Polynucleotide according to claim 29, wherein said microbial cell is a eukaryotic microbial cell.

31. Polynucleotide according to claim 30, wherein said eukaryotic microbial cell is selected from the group of eukaryotic cells consisting of fungal cells and a yeast cells.

32. Polynucleotide according to claim 31, wherein said eukaryotic microbial cell is a fungal cell, including a filamentous fungal cell.

33. Polynucleotide according to claim 32, wherein said fungal cell is a dimorphic fungal cell.

34. Polynucleotide according to claim 32, wherein said fungal cell belongs to the class of Zygomycetes.

35. Polynucleotide according to claim 32, wherein said fungal cell belongs to the order of Mucorales.

36. Polynucleotide according to claim 32, wherein said fungal cell belongs to the genus selected from the group of genera consisting of Mucor, Mycotypha, and Cokeromyces.

37. Polynucleotide according to claim 32, wherein said fungal cell belongs to the genus Mucor.

38. Polynucleotide according to claim 37, wherein said fungal cell is a Mucor species selected from the group of Mucor species consisting of M. circinelloides; M. rouxii, M. genevensis, M. bacilliformis, and M. subtillissimus.

39. Polynucleotide according to claim 37, wherein the Mucor species is M. circinelloides.

40. Polynucleotide according to claim 1, wherein the second nucleotide sequence comprising an expression signal comprises at least one element of a promoter region capable of being regulated, including being induced or repressed, during growth of the dimorphic fungal cell, by any one or more factors including

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof,

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell.

41. Polynucleotide according to claim 40, wherein the induction, derepression or repression of the expression of the first nucleotide sequence being operably linked to the expression signal is an induction or a repression of said expression, as compared to a predetermined expression level, by at least a factor of 2.0.

42. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal is regulated, during growth of the dimorphic fungal cell, by the carbon source of the growth medium.

43. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal is regulated, during growth of the dimorphic fungal cell, by the oxygen content and the carbon source of the growth medium.

44. Polynucleotide according to claim 40, wherein the expression of the first nucleotide sequence being operably linked to the expression signal comprising the at least one element of the promoter region is induced by the presence in the growth medium, or the addition to the growth medium, of a carbon source.

45. Polynucleotide according to claim 44, wherein the carbon source comprises a hexose

46. Polynucleotide according to claim 45, wherein the carbon source is selected from glucose and galactose.

47. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 741 of SEQ ID NO:9,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *gpd1* of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14066; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:9, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:9; and

iv) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:9,

and the complementary strand of such a polynucleotide.

48. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 741 of SEQ ID NO:9, or a fragment thereof, wherein said fragment is capable of directing gene expression in a dimorphic fungal cell and is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:9.

49. Polynucleotide according to claim 48, wherein said factor is selected from the group consisting of

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell.

50. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 741 of SEQ ID NO: 9, or the promoter region of *gpd1* of M. circinelloides, as deposited with DSMZ under accession number DSM 14066.

51. Polynucleotide according to claim 40, wherein at least one element of the promoter region comprised by the expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 755 of SEQ ID NO:10,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *prnC* of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14067; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:10, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by nucleotides 1 to 755 of SEQ ID NO:10; and

iv) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by nucleotides 1 to 755 of SEQ ID NO:10,

and the complementary strand of such a polynucleotide.

52. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 755 of SEQ ID NO:10, or a fragment thereof, wherein said fragment is capable of directing gene expression in a dimorphic fungal cell and is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by nucleotides 1 to 755 of SEQ ID NO:10.

53. Polynucleotide according to claim 52, wherein said factor is selected from the group consisting of

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell.

54. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 755 of SEQ ID NO: 10, or the promoter region of *prnC* of M. circinelloides, as deposited with DSMZ under accession number DSM 14067.

55. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 927 of SEQ ID NO:13,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *tubA* of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14841; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:13, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:13; and

iv) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:13,

and the complementary strand of such a polynucleotide.

56. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 927 of SEQ ID NO:13, or a fragment thereof, wherein said fragment is capable of directing gene expression in a dimorphic fungal cell and is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:13.

57. Polynucleotide according to claim 56, wherein said factor is selected from the group consisting of

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight

compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell.

58. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 927 of SEQ ID NO: 13, or the promoter region of *tubA* of M. circinelloides, as deposited with DSMZ under accession number DSM 14841.

59. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 419 of SEQ ID NO:14,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *gal1* of Mucor circinelloides, as deposited with EMBL under accession number AJ438267; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:14, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:14; and

iv) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:14,

and the complementary strand of such a polynucleotide.

60. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 419 of SEQ ID NO:14, or a fragment thereof, wherein said fragment is capable of directing gene expression in a dimorphic fungal cell and is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:14.

61. Polynucleotide according to claim 60, wherein said factor is selected from the group consisting of

i) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof

ii) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

iii) the growth phase of the dimorphic fungal cell, and

iv) the growth rate of the dimorphic fungal cell.

62. Polynucleotide according to claim 40, wherein the at least one element of the promoter region comprised by the expression signal comprises nucleotides 1 to 419 of SEQ ID NO: 14, or the promoter region of *gal1* of M. circinelloides, as deposited with EMBL under accession number AJ438267.

63. Polynucleotide according to claim 1 and operably linked to a further polynucleotide selected from the group of polynucleotides consisting of a 3' untranslated region, or a fragment thereof, and/or a 5' upstream region, or a fragment thereof.

64. Polynucleotide according to claim 1, wherein the at least one regulator of morphology is a polypeptide capable of regulating gene transcription in a dimorphic fungal cell by forming an interaction with a recognition motif of a promoter region having an affinity for the at least one regulator of morphology.

65. Polynucleotide according to claim 1, wherein the expression of said first polynucleotide results in the production of the at least one regulator in an increased or decreased amount, as compared to the amount of regulator produced, when the first polynucleotide encoding the at least one regulator is operably linked to the native promoter region under substantially identical growth conditions, and wherein the expression of said first polynucleotide and the production of the at least one regulator in an increased or a decreased amount results in an improved filamentation, or in a dimorphic shift of the dimorphic fungal cell.

66. Polynucleotide according to claim 65, wherein an increased amount of the at least one regulator of morphology is produced from the expression of the first nucleotide sequence encoding said regulator.

67. Polynucleotide according to claim 65, wherein a decreased amount of the at least one regulator of morphology is produced from the expression of the first nucleotide sequence encoding said regulator.

68. Polynucleotide according to claim 65, wherein the amount of regulator produced is increased or decreased at least by a factor of 2.0.

69. Polynucleotide according to claim 65, wherein the at least one regulator of morphology is a polypeptide encoded by a first polynucleotide comprising a first polynucleotide sequence forming part of a cAMP-dependent signal transduction pathway of a microbial cell, including a fungal cell, including a Mucor species, including M. circinelloides,

wherein the expression of said first polynucleotide results in the production of the at least one regulator in an increased or decreased amount, as compared to the amount of regulator produced, when the first polynucleotide encoding the at least one regulator is operably linked to the native promoter region under substantially identical growth conditions,

wherein the expression of said first polynucleotide and the production of the at least one regulator in an increased or a decreased amount results in an improved filamentation, or in a dimorphic shift of the dimorphic fungal cell.

70. Polynucleotide according to claim 65, wherein the at least one regulator of morphology is a polypeptide encoded by a first polynucleotide comprising a first polynucleotide sequence forming part of a MAP kinase-dependent signal transduction pathway of a microbial cell, including a fungal cell, including a Mucor species, including M. circinelloides,

wherein the expression of said first polynucleotide results in the production of the at least one regulator in an increased or decreased amount, as compared to the amount of regulator produced, when the first polynucleotide encoding the at least one regulator is operably linked to the native promoter region under substantially identical growth conditions,

wherein the expression of said first polynucleotide and the production of the at least one regulator in an increased or a decreased amount results in an improved filamentation, or in a dimorphic shift of the dimorphic fungal cell.

71. Polynucleotide according to claim 65, wherein the dimorphic shift of the dimorphic fungal cell is a shift from a first morphological condition of the dimorphic fungal cell characterised by a unicellular, essentially spherical morphology, to a second morphological condition of the dimorphic fungal cell, wherein the fungal cell comprises a mycelium and is characterised by filamentous growth.

72. Polynucleotide according to claim 65, wherein the dimorphic shift of the dimorphic fungal cell is a shift from a second morphological condition of the dimorphic fungal cell, wherein the fungal cell comprises a mycelium and is characterised by filamentous growth, to a first morphological condition of the dimorphic fungal cell characterised by a unicellular, essentially spherical morphology.

73. Polynucleotide according to any of claims 71 and 72, wherein the first morphological condition of the fungal cell characterised by a unicellular, essentially spherical morphology is further characterised by an essentially isodiametrical or spherical shape of the fungal cells.

74. Polynucleotide according to any of claims 71 and 72, wherein the second morphological condition of the dimorphic fungal cell, wherein the fungal cell comprises a mycelium and is characterised by filamentous growth, is further characterised by an essentially elongated, hyphal cell shape resulting from a polarised growth of a fungal cell characterised by the first morphological condition.

75. An isolated polypeptide capable of regulating the morphology of a dimorphic fungal cell and encoded by the first nucleotide sequence of claim 1.

76. An isolated polypeptide according to claim 75 comprising or essentially consisting of the amino acid sequence of SEQ ID NO:2, or a fragment thereof, or a

polypeptide functionally equivalent to SEQ ID NO: 2, or a fragment thereof, wherein said fragment or functionally equivalent polypeptide

a) has Mucor circinelloides protein kinase A regulatory subunit acitivty and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a cAMP binding domain of Mucor circinelloides protein kinase A, wherein said cAMP binding domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:2; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:2 for binding to at least one predetermined binding partner, including cAMP and/or PKAC.

77. An isolated polypeptide according to claim 75 comprising or essentially consisting of the amino acid sequence of SEQ ID NO:12, or a fragment thereof, or a polypeptide functionally equivalent to SEQ ID NO: 12, or a fragment thereof, wherein said fragment or functionally equivalent polypeptide

a) has Mucor circinelloides catalytic subunit of protein kinase A activity and is a regulator of morphology of a dimorphic fungal cell; and/or

b) is recognised by an antibody, or a binding fragment thereof, which is capable of recognising a protein kinase A binding domain of Mucor circinelloides PKAC, wherein said domain is comprised by the polypeptide having the amino acid sequence as shown in SEQ ID NO:12; and/or

c) is competing with a polypeptide comprising or essentially consisting of the amino acid sequence as shown in SEQ ID NO:12 for binding to at least one predetermined binding partner, including PKAR.

78. Polypeptide according to claim 75, wherein a substantially identical morphological shift is obtained from the production in a dimorphic fungal cell, under substantially identical conditions, of substantially identically amounts of i) the polypeptide comprising the at least one regulator of morphology of a dimorphic fungal cell, and ii) a functionally equivalent polypeptide comprising a functionally equivalent regulator of morphology, including any fragments thereof.

79. Polypeptide according to claim 78, wherein the functionally equivalent polypeptide, or a fragment thereof, comprises at least one conservative amino acid substitution.

80. A extrachromosomal, recombinant DNA molecule, preferably in the form of an expression vector, comprising the polynucleotide according to any of claims 1 to 74.

81. Recombinant DNA molecule according to claim 80 and further comprising a selectable marker.

82. A fungal host cell transfected or transformed with the polynucleotide according to any of claims 1 to 74, or the vector according to any of claims 80 and 81.

83. Fungal host cell according to claim 82, wherein said host organism is a dimorphic fungal cell.

84. Fungal cell according to claim 82 or dimorphic fungal cell according to claim 83, wherein said fungal cell or said dimorphic cell further comprises

i) at least one nucleotide sequence encoding a gene product, and operably linked thereto, and

ii) at least one further nucleotide sequence comprising a further expression signal capable of directing the expression in a dimorphic fungal cell of the at least one nucleotide sequence encoding the gene product, wherein

said further expression signal is regulatable, during growth of the dimorphic fungal cell, by one or more of

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof,

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell.

wherein the nucleotide sequence encoding the gene product and the further nucleotide sequence comprising the regulatable expression signal are not natively associated.

85. Dimorphic fungal cell comprising

i) at least one nucleotide sequence encoding a gene product, and operably linked thereto, and

ii) at least one further nucleotide sequence comprising a further expression signal capable of directing the expression in a dimorphic fungal cell of the at least one nucleotide sequence encoding the gene product, wherein said further expression signal is regulatable, during growth of the dimorphic fungal cell, by one or more of

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH,

low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof,

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell,

wherein the nucleotide sequence encoding the gene product and the further nucleotide sequence comprising the regulatable expression signal are not natively associated.

86. Dimorphic fungal cell according to claim 85 transfected or transformed with the polynucleotide according to any of claims 1 to 74, or the vector according to any of claims 80 and 81.

87. Dimorphic fungal cell according to claim 83, wherein the fungal cell belongs to the class of Zygomycetes.

88. Dimorphic fungal cell according to claim 87, wherein the fungal cell belongs to the order of Mucorales.

89. Dimorphic fungal cell according to claim 87, wherein the fungal cell belongs to a genus selected from the group of genera consisting of Mucor, Thermomucor, Rhizomucor, Mycotypha, Rhizopus, and Cokeromyces.

90. Dimorphic fungal cell according to claim 89, wherein the fungal cell belongs to the genus Mucor.

91. Dimorphic fungal cell according to claim 90, wherein the fungal cell belongs to a Mucor species selected from the group of Mucor species consisting of M.

circinelloides; M. hiemalis, M. rouxii, M. genevensis, M. bacilliformis, and M. subtillissimus.

92. Dimorphic fungal cell according to claim 91, wherein the Mucor species is M. circinelloides.

93. Dimorphic fungal cell according to claim 85, wherein the fungal cell belongs to the class of Zygomycetes.

94. Dimorphic fungal cell according to claim 93, wherein the fungal cell belongs to the order of Mucorales.

95. Dimorphic fungal cell according to claim 93, wherein the fungal cell belongs to a genus selected from the group of genera consisting of Mucor, Thermomucor, Rhizomucor, Mycotypha, Rhizopus, and Cokeromyces.

96. Dimorphic fungal cell according to claim 95, wherein the fungal cell belongs to the genus Mucor.

97. Dimorphic fungal cell according to claim 96, wherein the fungal cell belongs to a Mucor species selected from the group of Mucor species consisting of M. circinelloides; M. hiemalis, M. rouxii, M. genevensis, M. bacilliformis, and M. subtillissimus.

98. Dimorphic fungal cell according to claim 97, wherein the Mucor species is M. circinelloides.

99. Dimorphic fungal cell according to claim 85, wherein the at least one further nucleotide sequence comprising the further expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 741 of SEQ ID NO:9,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *gpd1* of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14066; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:9, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:9; and

iv) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:9,

and the complementary strand of such a polynucleotide.

100. Dimorphic fungal cell according to claim 85, wherein the at least one further nucleotide sequence comprising the further expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 755 of SEQ ID NO:10,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *prnC* of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14067; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:10, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:10; and

iv) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:10,

and the complementary strand of such a polynucleotide.

101. Dimorphic fungal cell according to claim 85, wherein the at least one further nucleotide sequence comprising the further expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 927 of SEQ ID NO:13

ii) a polynucleotide comprising or essentially consisting of the promoter region of the *tubA* gene of Mucor circinelloides, as deposited with DSMZ under accession number DSM 14841; and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:13, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:13; and

iii) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:13,

and the complementary strand of such a polynucleotide.

102. Dimorphic fungal cell according to claim 85, wherein the at least one further nucleotide sequence comprising the further expression signal is selected from the group consisting of

i) a polynucleotide comprising nucleotides 1 to 419 of SEQ ID NO:14,

ii) a polynucleotide comprising or essentially consisting of the promoter region of *gal1* of Mucor circinelloides, as deposited with EMBL under accession number AJ438267, and

iii) a polynucleotide comprising at least one fragment of SEQ ID NO:14, wherein said fragment

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

c) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:14; and

iii) a polynucleotide, the complementary strand of which hybridizes, under stringent conditions, with a polynucleotide as defined in any of (i), (ii) and (iii), wherein said polynucleotide

a) is capable of directing gene expression in a dimorphic fungal cell; and/or

b) is regulatable, during growth of the dimorphic fungal cell, by at least one factor capable of regulating gene expression directed by SEQ ID NO:14,

and the complementary strand of such a polynucleotide.

103. Dimorphic fungal cell according to claim 85, wherein the expression in the dimorphic fungal cell of the nucleotide sequence encoding the gene product results in the production of an increased amount of the gene product as compared to the production of the gene product in an at least substantially identical dimorphic fungal cell under substantially identical conditions, when the nucleotide sequence encoding the gene product is operably linked to the expression signal natively associated therewith.

104. Dimorphic fungal cell according to claim 103, wherein the amount of the gene product is increased by a factor of at least 1.25.

105. Dimorphic fungal cell according to claim 103, wherein the nucleotide sequence encoding a gene product and/or the further nucleotide sequence comprising an expression signal is derived from a fungal cell.

106. Dimorphic fungal cell according to claim 103, wherein the gene product is secreted into the growth medium.

107. Dimorphic fungal cell according to claim 103, wherein the gene product is selected from the group of gene products consisting of catalase, laccase, phenoloxidase, oxidase, oxidoreductases, cellulase, xylanase, peroxidase, lipase, hydrolase, esterase, cutinase, protease and other proteolytic enzymes, aminopeptidase, carboxypeptidase, phytase, lyase, pectinase and other pectinolytic enzymes, amylase, glucoamylase, alpha-galactosidase, beta-galactosidase, alpha-glucosidase, beta-glucosidase, mannosidase, isomerase, invertase, transferase, ribonuclease, chitinase, mutanase and deoxyribonuclease.

108. Dimorphic fungal cell according to claim 83 comprising i) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:11, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:9, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell, said cell further comprising ii) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:1, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:14, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell.

109. Dimorphic fungal cell according to claim 83 comprising i) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:11, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal

cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:13, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell, said cell further comprising ii) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:1, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:14, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell.

110. Dimorphic fungal cell according to claim 83 comprising i) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:11, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:13, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell, said cell further comprising ii) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:1, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:10, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell.

111. Dimorphic fungal cell according to claim 83 comprising i) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:11, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:9, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell, said cell further comprising ii) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:1, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:10, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell.

112. Dimorphic fungal cell according to claim 83 comprising i) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:11, or a

fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:14, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell, said cell further comprising ii) a first nucleotide sequence comprising the coding sequence of SEQ ID NO:1, or a fragment thereof encoding a regulator of morphology of said dimorphic fungal cell, said first sequence being operably linked to a second nucleotide sequence comprising SEQ ID NO:10, or a fragment thereof capable of directing gene expression in said dimorphic fungal cell.

113. Dimorphic fungal cell according to claim 83, wherein said cell comprises a replicon harbouring a selectable marker conferring resistance against an antibiotic.

114. Dimorphic fungal cell according to claim 113, wherein said antibiotic is geneticin.

115. Dimorphic fungal cell according to claim 113, wherein said replicon is capable of undergoing extrachromosomal replication in a bacterial cell.

116. Dimorphic fungal cell according to claim 113, wherein said replicon comprises SEQ ID NO:9, or a fragment thereof capable of directing gene expression.

117. Dimorphic fungal cell according to claim 113, wherein said replicon can be maintained at about 0.5 copies per nucleus at a first predetermined concentration of antibiotic, and maintained at about 2 to 50 copies per nucleus at a second and higher predetermined concentration of antibiotica.

118. Method for constructing a recombinant fungal cell according to claim 82, or a recombinant dimorphic fungal cell according to claim 83, said method comprising the step of transforming or transfecting a polynucleotide according to any of claims 1 to 74, or the vector of any of claims 80 and 81, into a fungal cell or a dimorphic fungal cell.

119. A method of claim 118 and comprising the further step of transforming or transfecting said recombinant fungal cell or said recombinant dimorphic fungal cell with a further polynucleotide comprising

i) at least one nucleotide sequence encoding a gene product, and operably linked thereto, and

ii) at least one further nucleotide sequence comprising a further expression signal capable of directing the expression in a dimorphic fungal cell of the at least one nucleotide sequence encoding the gene product, wherein said further expression signal is regulatable, during growth of the dimorphic fungal cell, by one or more of

a) the composition of the growth medium, including at least one of carbon source, nitrogen source including amino acids or precursors thereof, oxygen content, ionic strength, including NaCl content, pH, low molecular weight compounds, cAMP, and the presence or absence of a cell constituent, or a precursor thereof,

b) the temperature of the growth medium, including any change thereof, including an upshift eliciting the expression of one or more heat shock genes,

c) the growth phase of the dimorphic fungal cell, and

d) the growth rate of the dimorphic fungal cell,

wherein the nucleotide sequence encoding the gene product and the further nucleotide sequence comprising the regulatable expression signal are not natively associated.

120. Method for regulating the morphology of a recombinant fungal cell according to claim 82, or a recombinant dimorphic fungal cell according to claim 83, said method comprising the steps of

i) cultivating said fungal cell or said dimorphic fungal cell under conditions allowing expression of said first nucleotide sequence encoding the at least one regulator of morphology, and

ii) regulating the morphology of said recombinant fungal cell or said recombinant dimorphic fungal cell.

121. Method for obtaining a predetermined dimorphic shift of a dimorphic fungal cell according to any of claims 83 or 86, said method comprising the steps of

i) cultivating said dimorphic fungal cell under conditions allowing expression of said first nucleotide sequence encoding the at least one regulator of morphology, and

ii) obtaining a predetermined dimorphic shift of said dimorphic fungal cell, wherein said dimorphic shift results from regulating the expression in said dimorphic cell of said regulator of morphology.

122. Method for increasing the filamentation of a dimorphic fungal cell according to any of claims 83 or 86, said method comprising the steps of

i) cultivating said dimorphic fungal cell under conditions allowing expression of said first nucleotide sequence encoding the at least one regulator of morphology, and

ii) increasing the filamentation of said dimorphic fungal cell, wherein said increased filamentation results from regulating the expression in said dimorphic cell of said regulator of morphology.

123. Method for increasing the secretory capacity of a dimorphic fungal cell according to any of claims 83 or 86, said method comprising the steps of

i) cultivating said dimorphic fungal cell under conditions allowing expression of said first nucleotide sequence encoding the at least one regulator of morphology, and

ii) increasing the secretory capacity of said dimorphic fungal cell, wherein said increased secretory capacity results from regulating the expression in said dimorphic cell of said regulator of morphology.

124. Method for producing a gene product in a dimorphic fungal cell according to claim 86, said method comprising the steps of

i) cultivating said dimorphic fungal cell under conditions allowing expression of said first nucleotide sequence encoding said at least one regulator of morphology, and

ii) cultivating said dimorphic fungal cell under conditions allowing expression of said nucleotide sequence encoding said gene product, and

iii) producing a gene product.